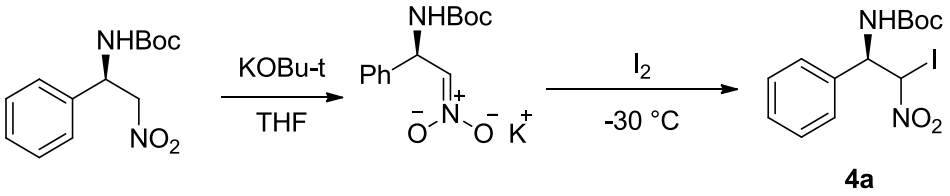
Contents

1. General Information

Glassware was oven-dried at 120 ℃ for all non-aqueous reactions. All reagents and solvents were commercial grade and purified prior to use when necessary. Acetonitrile (CH_3CN), toluene, and tetrahydrofuran (THF) were dried by passage through a column of activated alumina. Analytical thin-layer chromatography (TLC) was performed using E. Merck Silica gel 60 F254 pre-coated plates. Column chromatography was performed using 40-50 μm Silica Gel 60N (Kanto Chemical Co., Inc.). ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) spectra were recorded on an Agilent 400MR spectrometer. Chemical shifts are reported in (ppm) down field from tetramethylsilane with reference to solvent signals [^{1}H NMR: $CHCl_3$ (7.26), ^{6}d-DMSO (2.50); ^{13}C NMR: $CDCl_3$ (77.16), ^{6}d-DMSO (40.00)]. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak, coupling constant (Hz), integration and assignment. Infrared (IR) spectra were recorded on a PERKIN ELMER Spectrum BX FT-IR System spectrometer. High resolution mass spectra were measured on Themo Fisher Scientific Orbitrap Discovery (ESI LTQ Orbitrap).

2. Preparing starting materials or key intermediates



Scheme S-1. Synthesis of α-iodonitroalkane **4a**

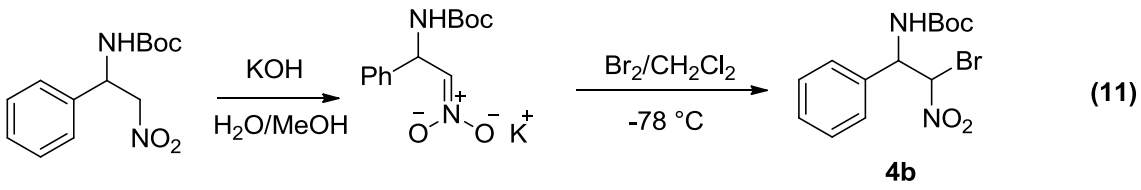
4a: Under Ar, nitroalkane (*R*)-**1**(532 mg, 2.0mmol) was dissolved in THF (10 mL). The reaction mixture was cooled to 0 ℃ and $KOBu^t$ (224 mg, 2 mmol) was added. After 30 min, a white precipitation formed and cooling to -30 ℃, I_2 (538 mg, 2.0 mmol) was added in one-portion. After a further 30 min, the reaction was quenched with *sat.* NH_4Cl solution (20 mmol) and extracted with CH_2Cl_2. The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to give crude **4a**, which was columned via silica gel chromatography (Hex/EA = 5/1) to give pure **4a** (470mg, 60%) as a white solid (stored at low temperature without light).

^{1}H NMR (400 MHz, $CDCl_3$, 1:1.67 mixture of diastereomers**)**: δ 1.45, 1.47 (s, 9H), 5.23-5.33, 5.97(m, 2.0H), 6.59-6.61 (m, 1H), 7.27-7.41 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz, 1:1.67 mixture of diastereomers**)**: δ 28.15, 28.20, 58.07, 81.01, 81.61, 85.20, 126.78, 126.97, 128.50, 129.01, 129.09, 129.13, 129.24, 129.54, 134.69, 135.25, 154.47, 154.74.

IR (neat): 3375, 1682, 1552, 1519, 1171 cm^{-1}.

HRMS (ESI) *m/z* calcd. for$C_{13}H_{17}IN_2NaO_4$ $(M+Na)^+$415.0125; found: 415.0133.



Scheme S-2. Synthesis of α-Bromo nitroalkane **4b**

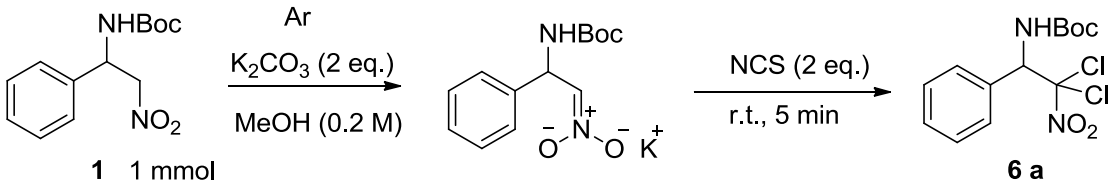
4b:[7] Under Ar, the nitroalkane **1** (532 mg, 2 mmol) was dissolved in KOH solution [116 mg KOH in H_2O (6 mL) + MeOH(2 mL)] until the white solid disappeared. The resulting solution was cooled until it started to freeze and then bromine (324 mg, mmol) in 10 mL of CH_2Cl_2 (pre-cooled to -78 ℃) was added, all at once, with vigorous stirring. After about 1 min, the layers are separated and the aqueous phase was extracted with 10 mL of CH_2Cl_2. The combined methylene chloride solutions were washed with 10 mL of H_2O and dried over anhydrous magnesium sulfate, and then the solvent was removed to give crude **4b**; further purification by silica gel chromatography (Hex/EA = 5/1) gave pure **4b** (552 mg, 80 %) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$, 1:1.4 mixture of diastereomers**)**: δ 1.43, 1.44(s, 9H,), 5.41-5.43 (m, 1H), 5.64-5.74 (m, 1H), 6.30 (s, 1H), 7.24-7.41 (m, 5H).

^{13}C NMR (**$CDCl_3$, 100 MHz,** 1:1.4mixture of diastereomers): δ 28.15, 28.20, 58.07, 81.03, 81.62, 85.23, 126.76, 126.95, 129.09, 129.13, 129.25, 134.68, 135.22, 154.72.

IR (neat): 3356, 1691, 1566, 1517, 1367, 1166, 699.

HRMS (ESI)*m/z* calcd. for $C_{13}H_{17}BrN_2NaO_4$ $(M+Na)^+$ 367.0264; found: 367.0273.



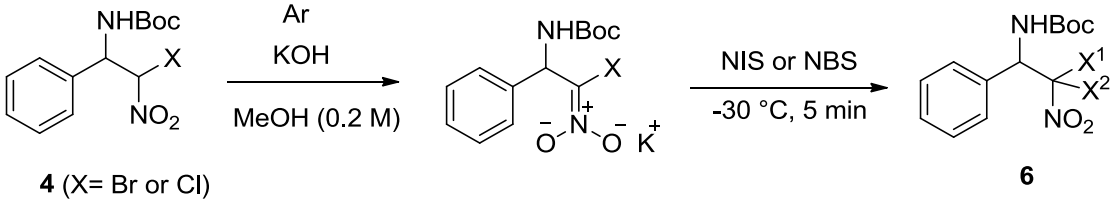
Scheme S-3. Synthesis of di-chloro nitroalkane **6a**

6a: Nitroalkane **1** (1 mmol) was dissolved in methanol (5 mL) in a two necked flask. The flask was degassed using freeze-pump-thaw techniques and backfilled with nitrogen (3 cycles). Next, KOH (1.5 eq.) was added in one portion at R.T. and the reaction stirred for 10 min. NCS (2.2 eq.) was added in one portion and stirring continued for 10 min. The mixture was then quenched with *sat.* NH_4Cl (30 mL) and extracted with CH_2Cl_2 (25×2mL). The organic phase was dried over $MgSO_4$, and concentrated under reduced pressure. Crude product was purified by flash column chromatography (ethyl acetate / hexane = 1 / 5) to give **6a** (white solid, yield = 81 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 9H), 5.60 (br s, 1H), 5.96 (br d, *J* = 9.2 Hz, 1H), 7.37-7.44 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.25, 63.88, 81.59, 116.08, 128.78, 128.96, 129.79, 133.25, 154.11.

HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}Cl_2N_2NaO_4$ $(M+Na)^+$ 357.0385, 359. 0355; found: 357.0379, 359.0348.

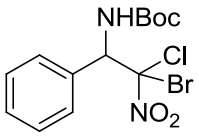


4 (X= Br or Cl) **6**

Scheme S-4A. Synthesis of di-halo nitroalkane **6**

Procedure: Bromo nitroalkane **4b** (1 mmol) *or* chloro nitroalkane **4c** (1 mmol) was dissolved in methanol (5 mL) in a two necked flask; the flask was degassed using freeze-pump-thaw techniques and backfilled with nitrogen (3 cycles). Next, KOH (1.5

eq.) was added in one portion at 0 ℃ and the reaction stirred for 5 min. After cooling to -30 ℃ bath for 5-10 min, NIS or NBS (1.1 eq.) was added in one portion. Warming to 0 ℃ (over 5 min) produced some precipitate. The mixture was then quenched with *sat.* NH_4Cl (30 mL) and stirred rapidly until a lot of white solid was generated before extraction with CH_2Cl_2 (25×2mL, pre-cooled to -30 ℃). The organic phase was dried over $MgSO_4$ at -30 ℃ (over a MeOH cooling bath), quickly filtered and the soltion concentrated under reduced pressure. The crude product was purified by flash column chromatography (ethyl acetate/hexane = 1/5, pre-cooled to -30 ℃ for bromo / chloro iodo nitroalkane) to obtain relatively pure compound **6**. Further purification via recrystallizion (CH_2Cl_2 + Hexane) in refrigerator (-30 ℃) gave pure compounds **6**.

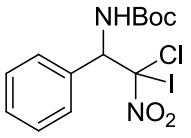


6b White solid, yield= 75 %.

^{1}H NMR (400 MHz, $CDCl_3$, 1:1.9 *syn*/*anti* mixture of diastereomers**)**: δ 1.41, 1.45 (s, 9H), 5.64-5.71 (m, 1 H), 5.98-6.00 (m, 1H), 7.33-7.47 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.23, 28.28, 64.38, 81.46, 104.46, 105.46, 128.65, 128.76, 128.96, 129.17, 129.69, 129.72, 133.11, 133.66, 153.93, 154.22.

HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}BrClN_2NaO_4$ $(M+Na)^+$ 400.9880, 402.9859; found: 400.9887, 402.9863.

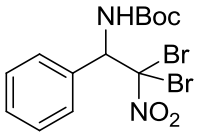


6c Yellow solid, yield= 60 %.

^{1}H NMR (400 MHz, $CDCl_3$, 1:2.25 *syn*/*anti* mixture of diastereomers**):** δ 1.42, 1.49 (s, 9H), 5.58, (d, J = 10.8 Hz, 0.78H), 5.80 (d, J = 10.0 Hz, 0.34H), 5.91 (d, J = 10.0 Hz, 0.31H), 6.06 (d, J = 10.4 Hz, 0.56H), 7.27-7.46 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.33, 28.42, 65.69, 75.95, 81.47, 128.68, 128.84, 128.97, 129.38, 129.61, 129.65, 132.36, 154.31.

HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}ClIN_2NaO_4$ $(M+Na)^+$ 448.9741; found: 448.9737.

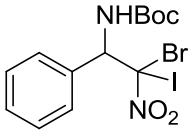


6d White solid, yield= 70 %.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (s, 9H), 5.6 (br s, 1H), 5.97 (br d, J = 9.2 Hz, 1H), 7.35-7.45 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.31, 64.71, 81.48, 94.54, 128.65, 129.16, 129.69, 133.77, 154.03.

HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}Br_2N_2NaO_4$ $(M+Na)^+$ 446.9354, 444.9375, 448.9334; found: 446.9349, 444.9370, 448.9326.

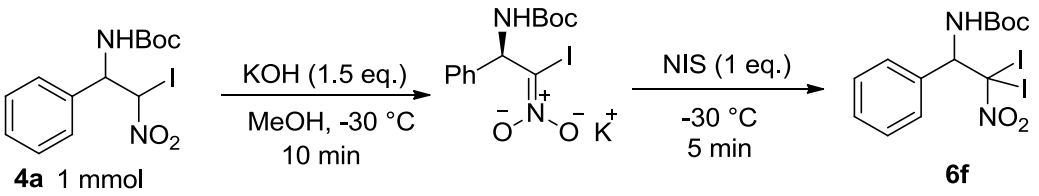


6e Yellow solid, yield= 60 %

^{1}H NMR (400 MHz, $CDCl_3$, 1:1.45 *syn*/*anti* mixture of diastereomers**):** δ 1.43, 1.48 (s, 9H), 7.31-7.48 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.19, 28.26, 64.90, 65.61, 65.91, 77.21, 81.27, 128.45, 128.56, 128.87, 129.25, 129.42, 129.55, 133.07, 153.68, 154.04.

HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}BrIN_2O_4$ $(M+Na)^+$ 492.9236, 494.9215; found: 492.9232, 494.9211.

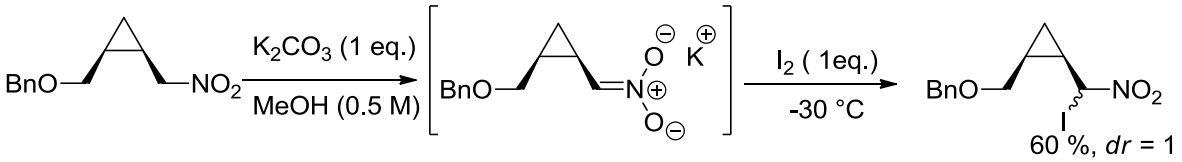


Scheme S-4B. Synthesis of di-iodo nitroalkane **6f**

6f: Iodo nitroalkane (1 mmol) was dissolved in methanol (5 mL) in a two-necked flask. The solution was degassed using freeze-pump-thaw techniques and backfilled with nitrogen (3 cycles). Next, KOH (1.5 eq.) was added in one portion at -30 ℃ and the reaction stirred for 10 min, at the same temperature, before NIS (1.5 eq.) was added and stirred continued for 3 min. The mixture was then quenched with *sat.* NH_4Cl (30 mL, pre-cooled to 0 ℃) and quickly stirred until copious amounts of white (sticky) solid was generated. The aqueous was then extracted with CH_2Cl_2 (25×2mL, pre-cooled to -30 ℃). The organic phase was dried over $MgSO_4$ (over a -30 ℃ MeOH bath), quickly filtrated and then concentrated under reduced pressure. The crude product was purified via recrystallization (CH_2Cl_2 + Hexane) in refrigerator (-30 ℃) to obtain relatively pure compound **6f** (yellow stickly solid, yield = 50 %)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (s,9H), 5.589 (d, J = 9.2 Hz, 1H), 5.733 (d, J = 8.4 Hz, 1H), 7.30-7.44 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.38, 61.19, 66.54, 81.40, 128.64, 129.13, 129.51, 131.10, 153.97.



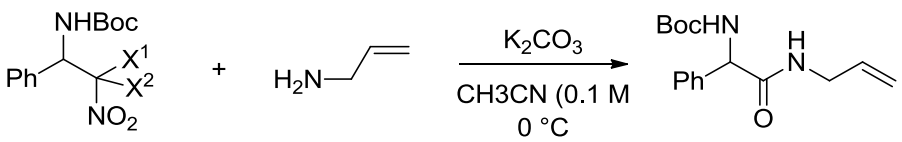
Scheme S-5. Synthesis of iodonitroalkane X

General procedure: Nitroalkane[13] (1.105g, 5 mmol) was dissolved in10 mL MeOH, then K_2CO_3 (1.035 g, 7.5 mmol) was added to stirred at R.T. for 10 min, then filter solid to collect solution. Cooling the solution to -30 , and added I_2 (1.27g, 5 mmol), slowly warm to 0, untile the solution become darken, then pour the reaction mixture to 100 mL water, and extract by CH_2Cl_2 (100 mL). The combined organic solution was dried over anhydrous magnesium sulfate, the solvent removed *in vacuo* and the crude product purified by silica gel chromatography to give the pure X (a *ca.* 1:1 mixture of diastereomers)

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.53-0.58 (m, 0.5 H), 0.81-0.85 (m, 0.5 H), 1.04-1.09 (m, 0.5 H), 1.14-1.19 (m, 0.5 H), 2.11-2.22 (m, 1H), 3.39 (dd, *J* = 3.6, 10.8 Hz, 0.5 H), 3.55 (dd, *J* = 5.6, 11.2 Hz, 0.5 H), 3.66 (dd, *J* = 4.0, 10.4 Hz, 0.5 H), 4.17-4.57 (m, 2H), 6.08 (d, *J* = 3.6 Hz, 0.5 H), 6.08-6.12 (m, 1H), 6.98-7.38 (m, 5H).

^{13}C NMR (400 MHz, $CDCl_3$): δ 11.09, 12.52, 18.44, 24.31, 24.51, 24.76, 52.23, 52.30, 66.07, 67.60, 73.15, 73.24, 127.83, 127.85, 127.88, 127.92, 128.46, 128.54, 137.50.

HRMS (ESI) *m/z* calcd. for $C_{12}H_{14}INNaO_3$ $(M+Na)^+$ 369.9911; found: 369.9901.



Scheme S-6. Di-halo nitroalkane react with allylamine

General procedure: To a two necked flask, nitroalkane (0.1 mmol) in 1.0 mL of CH_3CN, the solutions were first degassed (freeze-pump-thaw cycles), not using oxygen were performed under an argon atmosphere (balloon), whereas using oxygen were performed under an oxygen atmosphere (balloon). Then cooled to 0 ℃, allylamine (0.15 mmol) and base (0.15 mmol) were added by one-portion. After reaction finished , $CHCl_3$ was added to the reaction and the precipitate filtered through a short silica gel column. The crude product purified by silica gel chromatography (Hexane/Ethyl acetate = 3/1) to give the pure amide product.

(±)-tert-butyl 4-(allylamino)-4-oxo-3-phenylbutanoate(4)

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (s, 9H), 3.83-3.86 (m, 2H), 4.98-5.06 (m, 2H), 5.16 (br s, 1H), 5.69-5.79 (m, 1H), 5.84 (br s, 1H), 5.92 (br s, 1H), 7.30-7.35 (m, 5H).

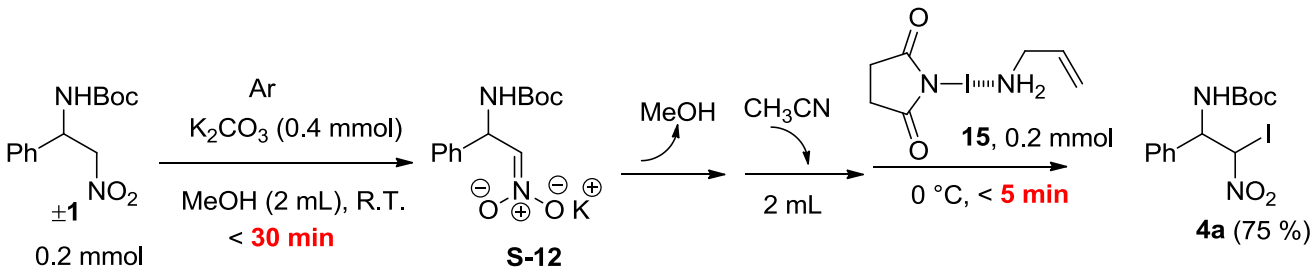
^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.43, 42.06, 58.62, 80.19, 116.44, 127.31, 128.45, 129.11, 133.72, 138.60, 155.34, 170.18.

IR (neat): 3312, 2976, 1700, 1654, 1522, 1497, 1364, 1249, 1169, 697.

HRMS (ESI): *m/z* calcd. for $C_{27}H_{34}N_2NaO_6$ $(M+Na)^+$ 313.1523; found:313.1555.

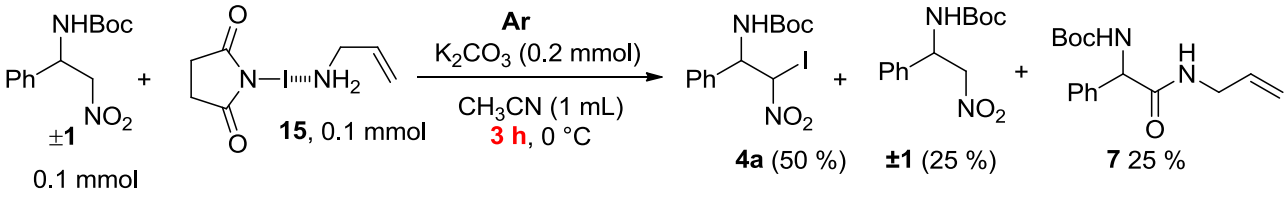
3. Mechanistic study

3.1 α-iodonitroalkane formation



Scheme S-7A. Formation of α-iodo nitroalkane **4a** using pre-generated anion.

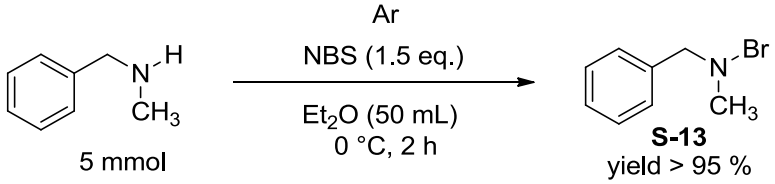
In order to show the NIS-amine complex **15** to be a source of electrophilic iodine, the nitroalkane **1** was deprotonated by K_2CO_3 to form anion **S-12** in methanol (**Scheme S-7A**). After 30 min, >95 % yield of anion **S-12** was generated. Subsequent removal of methanol, changing the solvent to CH_3CN, cooling to 0 ℃, adding the pre-prepared complex **15** in one-portion, stirring for <5 min, quenching with sat. NH_4Cl solution, and purifying the crude by silica gel chromatography afforded the α-iodo nitroalkane **4a** in 75 % yield.



Scheme S-7B. Formation of α-iodonitroalkane **4a** using in situ-generated anion.

Under O_2, the α-iodo nitroalkane reacts with the amine within 30 minutes. To check the intermediacy of α-iodonitroalkane **4a**, we conducted reactions of **1** with NIS-amine complex **15** under Ar in presence of K_2CO_3 (**Scheme S-7B**). After 3 h, about 50 % of α-iodo nitroalkane **7**, 25 % amide and 25 % of starting nitroalkane **1** were observed. These yields and reaction times are consistent with reactions under O_2.

3.1 N-bromo amine reaction with nitroalkane or *aci*-nitronate

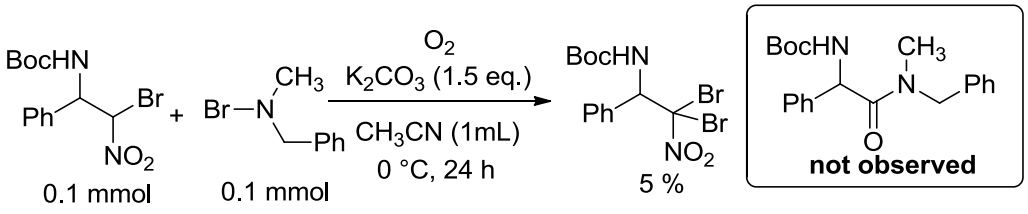


Scheme S-8. Preparing compound N-bromo amine[10,11]

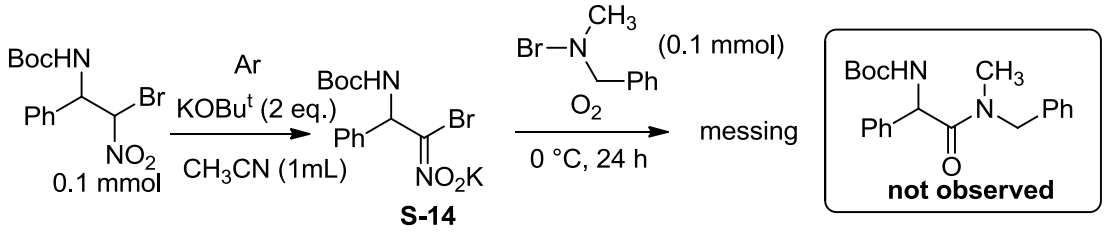
Procedure to prepare N-bromo amine: Under Ar, N-methyl benzylamine (5 mmol) was dissolved in 50 mL Et_2O, the flask was cooled down over an ice bath for 10 min before NBS was added in one-portion. The reaction was stirred at the same temperature for 2 h and the succinimide filtered off. Collection of the organic solution and evaporating off Et_2O (whilst immersing in an ice-water bath) *in vacuo* gave a thick yellow oil, which was found to be unstable and should be used immediately, or stored at low temperature, in a yield of about 95 %.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.10 (s, 3H), 4.07 (s, 2H), 7.32-7.36 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 54.23, 71.94, 128.12, 128.51, 129.19, 137.81.



Scheme S-9A; Reaction of N-bromo amine **4a** with in-situ generated anion



Scheme S-9B; Reaction of N-bromo amine **4a** with pre-generated anion

In order to check umpolung amide synthesis[6] existed for the amine component, we prepared N-bromo amine to react with the bromo nitroalkane in presence of K_2CO_3 (**Scheme S-9A**) under O_2. After 24 h, the reaction was diluted by $CHCl_3$ and the solid

salts removed through a short SiO_2 column. NMR of the crude, showed mostly bromo nitroalkane decomposition and trace amounts of dibromo nitroalkane were formed; amide products could not be confirmed nor isolated. In a separate experiment, the anion of the bromo nitroalkane was formed (by using $KOBu^t$ in CH_3CN under Ar) and was reacted directly with the freshly prepared N-bromo amine (**Scheme S-9B)**. Again, no amide was observed nor isolated and the starting bromo nitroalkane decomposed.

3.3 Reaction of α-iodo nitroalkanes with amine or NIS-complex

(**Scheme S-10, A**): The α-iodonitroalkane **4a** was mixed with amine in presence of K_2CO_3 (2 eq.) in CH_3CN at 0 ℃ under O_2. After 30 min, the reaction was diluted with $CHCl_3$ and the precipitate removed through a short silica gel plug. Further purification by gel silica gel chromatography gave the pure amide product **7** (yield = 74 %).

(**Scheme S-10**, **B**): The α-iodo nitroalkane **4a** was mixed with amine in presence of K_2CO_3 (2 eq.) in CH_3CN at 0 ℃ under Ar. After 3 h, the reaction was diluted with $CHCl_3$ and the precipitate removed through a short silica gel plug. The de-iodinated nitroalkane **1** and iodo nitroalkane **4a** and trace amounts of amide **7** were calculated to be in a ratio of **4a**:**1**: **7** = 42:40:18 by ^1H NMR analysis.

(**Scheme S-10**, **C**): The α-iodonitroalkane **4a** was mixed with K_3CO_3 under an O_2 atmosphere. After 15 mins, the α-iodonitroalkane **4a** reacted completely, as checked by TLC; after aqueous acid work-up, only the carboxylic acid **5** was isolated in 61 % yield.

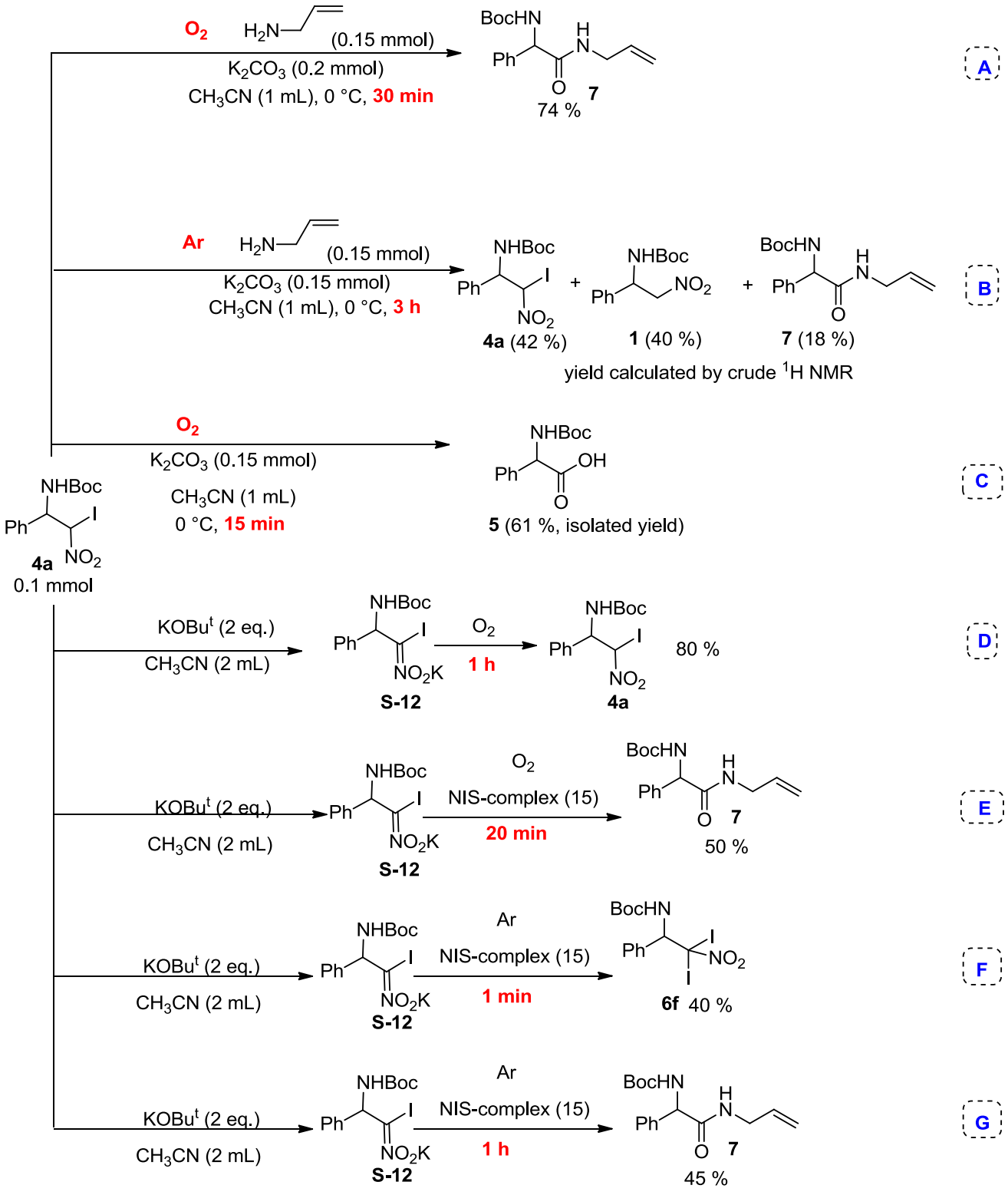
(**Scheme S-10**, **D**): The pre-formed pure anion **S-12** was prepared by reacting iodo

nitroakane with $KOBu^t$ (2 eq.) under Ar at -30 ℃ and the reaction system was saturated with O_2 atmosphere by freeze-thaw techniques. After 1h, the reaction was quenched with *sat.* NH_4Cl. Only the iodo nitroalkane **4a** was recovered.

(**Scheme S-10**, **E**): The pre-formed pure anion **S-12** was prepared by reacting iodo nitroakane with $KOBu^t$ (2 eq.) under Ar at -30 ℃ and the reaction system was saturated with O_2 atmosphere by freeze-thaw techniques. The NIS-complex **15** (1 eq.) was then added in one-portion at 0 ℃, at the same tempreture for 20 min, then reaction was diluted by $CHCl_3$ and further purify by silicane gel column chromatography (Hex/EA = 3/1), the amide **7** (50 %) was isolated.

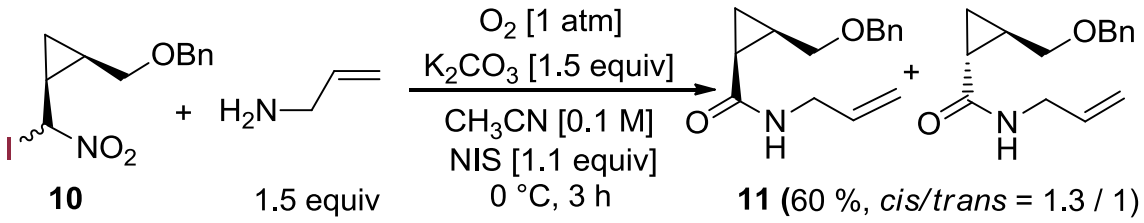
(**Scheme S-10**, **F**): The pre-formed pure anion **S-12** was prepared by reacting iodo nitroakane with $KOBu^t$ (2 eq.) under Ar at -30 ℃, then NIS-complex **15** (1.0 eq.) was added in one-portion. After 1 min, the reaction was quenched with cold *sat.* NH_4Cl (at -30 ℃ over a MeOH cooling bath). This gave 40 % di-iodo nitroalkane **6f** and recovered starting materials.

(**Scheme S-10**, **G**): The pre-formed pure anion **S-12** was prepared by reacting iodo nitroakane with $KOBu^t$ (2 eq.) under Ar at -30 ℃ and the reaction system was saturated with Ar atmosphere by freeze-thaw techniques. The NIS-complex **15** (1 eq.) was then added in one-portion at 0 ℃, at the same temperature for 1 h, then reaction was diluted by $CHCl_3$ and further purify by silicane gel column chromatography (Hex/EA = 3/1), the amide **7** (45 %) was isolated.



Scheme S-10 Reaction of α-iodonitroalkane

3.4 Radical clock reaction



Scheme S-11 Reaction of α-iodonitroalkane with allyl amine

Procedure: The iodo-nitroalkane **10** (0.1 mmol), K_2CO_3 (1.5 equiv), CH_3CN (1mL, pre-saturated with O_2) and allyl amine (0.15 mmol) were added to a 10 mL flask. The reaction mixture was then cooling to 0 ℃ before NIS (0.01 mol) was added, then the reaction put under an O_2-balloon atmosphere. After the iodonitroalkane **11** disappeared by TLC monitoring, $CHCl_3$ was added to the reaction and the precipitate filtered through a short silica gel column. The solvent removed *in vacuo* and the crude product purified via lash silica gel column chromatography (Hexane/Ethyl acetate = 3/2, *cis/ trans* = 1.3/1), *cis* and *trans* was determined by NOE.

HRMS (ESI): *m/z* calcd. for $C_{15}H_{19}NNaO_2$ $(M+Na)^+$ 268.1308; found: 268.1307.

***cis* product**: Rf = 0.45

^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93-0.99 (m, 1H), 1.08-1.12 (m, 1H), 1.47-1.60 (m, 2H), 3.52 (dd, J = 9.6, 10.0 Hz, 1H), 3.80 (dd, J = 5.2, 10.0 Hz, 1H), 3.84-3.88 (m, 2H), 4.44 (dd, J = 11.6, 14.4 Hz, 2H), 5.06-5.20 (m, 2H), 5.75-5.85(m, 1H), 5.89 (br s, 1H), 7.23-7.33 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 9.81, 19.57, 19.97, 42.15, 68.65, 72.94, 116.20, 127.50, 127.76, 128.28, 134.36, 138.41, 170.63.

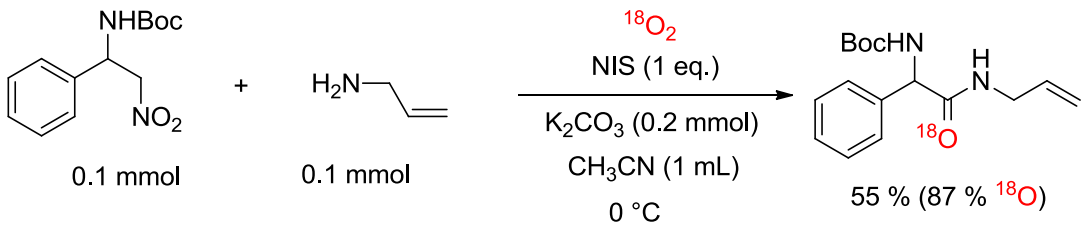
***trans* product**: R_f = 0.44

^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.73-0.77 (m, 1H), 1.18-1.23 (m, 1H), 1.28-1.32 (m,

1H), 1.62-1.76 (m, 1H), 3.31 (dd, J = 6.8, 10.4 Hz, 1H), 3.51 (dd, J = 5.6, 10.4 Hz, 1H), 3.81-3.94 (m, 2H), 4.50 (dd, J = 12.0, 15.2 Hz, 2H), 5.10-5.20 (m, 1H), 5.63 (br s, 1H), 5.78-5.88 (m, 1H), 7.24-7.35 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.83, 20.38, 42.18, 71.64, 72.55, 116.43, 127.63, 128.39, 134.33, 138.20, 172.19.

3.5 ^{18}O labeled reaction.



S-12. Nitroalkane reaction with amine under $^{18}O_2$

Procedure: The nitroalkane (0.1 mmol), K_2CO_3 (2.0 equiv), CH_3CN (1mL) and amine (0.1 mmol) were added to a 10 mL flask. The reaction mixture was then frozen under liquid nitrogen before NIS (0.1 mmol) was added and the reaction sealed with a glass septum screw cap and parafilm. The flask was degassed using three 10 minute freeze-pump-thaw cycles, after which the frozen solution was placed under high vacuum and the $^{18}O_2$ regulator needle was inserted through the septum. The vacuum line was closed and then the $^{18}O_2$ gas regulator was opened to fill the static vacuum. The flask was warmed to 0 ℃ and allowed to stir for 4.5 h before the reaction mixture was diluted with chloroform, filtered, and concentrated. The residue was purified via flash silica gel column chromatography.

^{18}O Percentage Mass Spectrometry Calculation

The amount of ^{18}O incorporation was determined as follows:

(^{16}O ion intensity) x (predicted ^{18}O ion natural abundance in the unlabeled compound)／100 =^{18}O ion intensity expected in the unlabeled compound

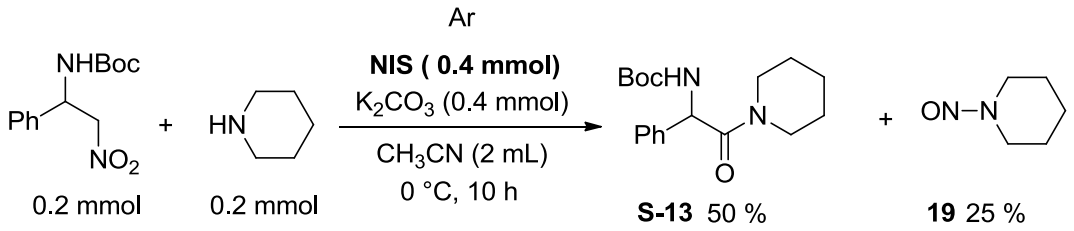
(^{18}O ion intensity) – (^{18}O ion intensity expected in the unlabeled compound) = corrected ^{18}O ion intensity ion intensity (Corrected ^{18}O ion intensity) / (Corrected ^{18}O ion intensity + ^{16}O ion intensity) x 100 = XX% (^{18}O incorporation)

^{18}O ion intensity expected in the unlabeled compound = 14.96 x 1.4 / 100 = 0.21

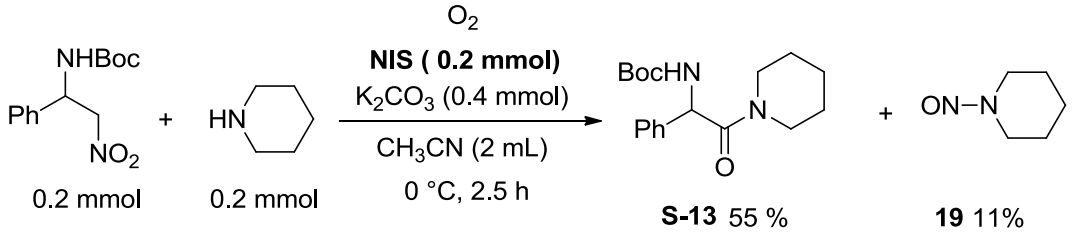
corrected ^{18}O ion intensity = 100 – 0.21 = 99.79

^{18}O incorporation = 99.79 / (99.79 + 14.96) x 100 = 87 %

3.6 Isolate N-nitroso amines



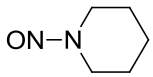
Scheme S-13A. Reaction under Ar



Scheme S-13B. Reaction under O_2

Procedure: To a reaction tube, the nitro-alkane (0.2 mmol), K_2CO_3 (0.4 mmol), amine (0.2 mmol), and dry CH_3CN (2 mL) were added. After freezing in liquid nitrogen, NIS (0.4 mmol) was added and the reaction was sealed with a glass septum screw cap and parafilm. After degassing using three 10 minute freeze-pump-thaw cycles, i.e.,

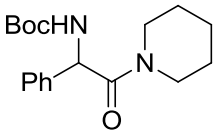
saturating the solution with either Ar or O_2, the solution was warmed over an ice-water bath for 5-10 min. After the nitroalkane disappeared as indicated by TLC, Et_2O was added to the reaction and the precipitate filtered through a short silica gel column. The combined organic solution was dried over anhydrous magnesium sulfate, the solvent removed *in vacuo*, and the crude product purified by silica gel chromatography (Et_2O/pentane = 1/2) to give the pure amide product **S-13** (yield =50 % under Ar; 55 % under O_2) and the N-nitroso amine **19** (yield =25 % under Ar; 11 % under O_2). NMR data were consistent with literature [12].



19

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.48-1.58 (m, 2 H), 1.72-1.84 (m, 4H), 3.77 (t, *J* = 6.0 Hz, 2H), 4.18 (t, *J* = 6.0 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.33, 24.91, 26.57, 39.94, 51.00.



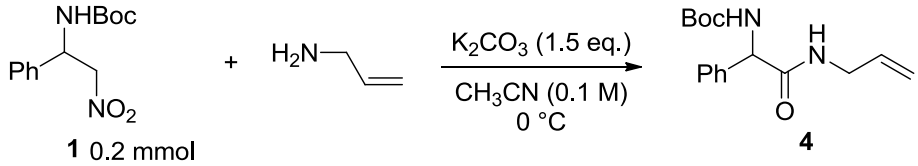
S-13

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84-0.94 (m, 1H), 1.25-1.43 (m, 3H), 1.40 (s, 9H), 1.47-1.54 (m, 2H), 3.21-3.29 (m, 2H), 3.37-3.46 (m, 1H), 3.67-3.73 (m, 1H), 5.53 (d, *J* = 8.0 Hz, 1H), 6.10 (d, *J* = 7.6 Hz, 1H), 7.23-7.36 (m, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.40, 25.49, 25.64, 28.50, 43.54, 46.53, 55.19, 79.65, 127.79, 128.11, 129.06, 138.75, 155.19, 168.12.

HRMS (ESI) *m/z* calcd. for $C_{18}H_{26}N_2NaO_3$ $(M+Na)^+$ 341.1836; found: 341.1835

4. The effect of halogen sources [a]



entry	NIS (mol %)	NIX-complex[c] (mol %)	other halogen source (mol %)	O_2[b] (1 atm)	time (h)	yield (%)
1	100			yes	4	66
2		100		yes	4	50
3		100		no	10	25
4		200		no	10	33
5	200			no	10	35
6			NCS (100)	yes	12	0
7			NBS (100)	yes	48	38
8	10		NBS (100)	yes	18	55
9			I_2 (100)	yes	4	38
10	100		I_2 (100)	no	10	26

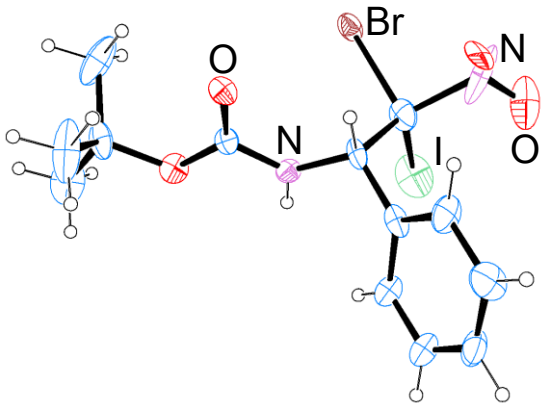
[a] Reactions were performed at 0.1 M of nitroalkane in 2.0 mL of CH_3CN with 1.0 equiv of allylamine; [b]All solutions were first degassed (freeze-pump-thaw cycles), and entries not using oxygen were performed under an argon atmosphere (balloon), whereas entries using oxygen were performed under an oxygen atmosphere (balloon). [c] Reaction performed without adding extra amine separately.

5. X-Ray crystal structure and data

Bromo iodo-nitroalkane 6 (X = I, Br)

The single crystal of **6 (X = I, Br)** suitable for X-ray analysis was grown in a solution of dichloromethane/Hexane at -30 ℃ under Ar; A colorless prism crystal of $C_{28}H_{32}Br_2I_2N_4O_8$ having approximate dimensions of 0.300 × 0.100 × 0.100 mm was

mounted on a glass fiber. All measurements were made on a Rigaku XtaLAB mini diffractometer using graphite monochromated Mo-K radiation. The crystal-to-detector distance was 50.00 mm. The data were collected at a temperature of -123 ± 1 ℃ to a maximum 2q value of 55.0 º. A total of 540 oscillation images were collected. The structure was solved by direct methods and expanded using Fourier techniques. Some non-hydrogen atoms were refined anisotropically, while the rest were refined isotropically. Crystallographic data has been deposited with the Cambridge Crystallographic Data Center, **CCDC reference number: 1054441**



EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{28}H_{32}Br_2I_2N_4O_8$
Formula Weight	966.20
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.300 X 0.100 X 0.100 mm
Crystal System	hexagonal
Lattice Type	Primitive
Lattice Parameters	a = 21.554(3) Å c = 15.8983(11) Å V = 6396.4(13) $Å^3$
Space Group	$P6_5$ (#170)
Z value	6
D_{calc}	1.505 g/cm^3
F_{000}	2808.00
m(MoKa)	33.962 cm^{-1}

B. Intensity Measurements

Diffractometer	XtaLAB mini
Radiation	MoKa (l = 0.71075 Å) graphite monochromated
Voltage, Current	50kV, 12mA
Temperature	-123.0°C
Detector Aperture	75.0 mm (diameter)
Data Images	540 exposures
w oscillation Range (c=54.0, f=0.0)	-60.0 - 120.0°
Exposure Rate	32.0 sec./°
Detector Swing Angle	30.00°
w oscillation Range (c=54.0, f=120.0)	-60.0 - 120.0°
Exposure Rate	32.0 sec./°
Detector Swing Angle	30.00°
w oscillation Range (c=54.0, f=240.0)	-60.0 - 120.0°
Exposure Rate	32.0 sec./°
Detector Swing Angle	30.00°
w oscillation Range (c=54.0, f=0.0)	-60.0 - 120.0°
Exposure Rate	32.0 sec./°
Detector Swing Angle	30.00°
w oscillation Range (c=54.0, f=120.0)	-60.0 - 120.0°
Exposure Rate	32.0 sec./°
Detector Swing Angle	30.00°
w oscillation Range (c=54.0, f=240.0)	-60.0 - 120.0°
Exposure Rate	32.0 sec./°
Detector Swing Angle	30.00°
Detector Position	50.00 mm
Pixel Size	0.073 mm
$2q_{max}$	55.0°
No. of Reflections Measured	Total: 67491 Unique: 9748 (R_{int} = 0.0522) Parsons quotients (Flack x parameter): 3780
Corrections	Lorentz-polarization Absorption (trans. factors: 0.358 - 0.712) Secondary Extinction (coefficient: 7.07000e-003)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR2008)
Refinement	Full-matrix least-squares on F^2
Function Minimized	S w $(Fo^2 - Fc^2)^2$
Least Squares Weights	w = 1/ [$s^2(Fo^2)$ + $(0.2000 \cdot P)^2$ + 0.0000 · P] where P = (Max(Fo^2,0) + 2Fc^2)/3
$2q_{max}$ cutoff	55.0°
Anomalous Dispersion	All non-hydrogen atoms

No. Observations (All reflections)	9748
No. Variables	388
Reflection/Parameter Ratio	25.12
Residuals: R1 (I>2.00s(I))	0.1084
Residuals: R (All reflections)	0.1166
Residuals: wR2 (All reflections)	0.3200
Goodness of Fit Indicator	1.425
Flack parameter (Parsons' quotients = 3780)	0.472(8)
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	5.69 $e^-/Å^3$
Minimum peak in Final Diff. Map	-2.49 $e^-/Å^3$

Table 1. Atomic coordinates and B_{iso}/B_{eq}

atom	x	y	z	B_{eq}
I2	0.64105(8)	0.23086(9)	0.25027(11)	4.80(4)
I33	0.46693(12)	-0.04374(12)	0.0057(2)	7.78(7)
Br1	0.47984(11)	0.00640(12)	0.20389(14)	3.92(4)
Br30	0.76104(7)	0.35020(7)	0.12158(8)	1.80(3)
O1	0.9019(6)	0.3068(6)	0.1663(8)	3.0(2)
O2	0.8255(6)	0.1963(7)	0.1149(9)	3.4(2)
O3	0.6797(7)	0.0921(6)	0.2179(9)	3.2(2)
O4	0.6770(7)	-0.0123(6)	0.1806(9)	3.5(2)
O26	0.8099(8)	0.4247(7)	0.3038(11)	4.1(3)
O29	0.6942(7)	0.3754(8)	0.3217(10)	3.8(2)
O35	0.4428(14)	0.0792(13)	0.008(2)	8.3(7)
O36	0.5144(12)	0.1452(9)	0.0875(11)	4.9(4)
N23	0.7922(7)	0.2356(7)	0.2246(9)	2.5(2)
N24	0.6214(8)	0.0276(7)	0.1013(9)	2.8(2)
N25	0.7467(8)	0.3734(7)	0.2973(9)	3.1(2)
N34	0.4842(13)	0.1023(17)	0.0669(17)	8.2(10)
C2	0.8464(9)	0.2516(10)	0.1675(9)	2.7(3)
C3	0.6267(9)	0.1055(8)	-0.0147(13)	3.1(3)
C4	0.7990(14)	0.2982(14)	0.5187(14)	4.5(4)
C5	0.5984(8)	0.0754(8)	0.0730(12)	2.9(3)
C6	0.8136(11)	0.3171(12)	0.4351(11)	3.4(3)
C7	0.7154(10)	-0.0150(11)	0.2558(17)	4.3(4)
C8	0.6766(15)	0.1606(14)	-0.1721(14)	4.7(4)
C9	0.7545(13)	0.2211(15)	0.5374(13)	4.4(4)
C10	0.6355(11)	0.0647(10)	-0.0786(12)	3.5(3)
C11	0.7290(13)	0.1760(16)	0.4813(15)	4.8(5)
C12	0.8711(12)	0.2006(15)	0.0457(15)	5.3(6)
C13	0.5124(11)	0.0392(13)	0.0787(16)	4.4(4)
C14	0.7885(15)	0.0492(10)	0.261(3)	7.5(10)
C15	0.8223(17)	0.1277(14)	0.0037(19)	6.1(7)
C16	0.7400(8)	0.3119(8)	0.2465(11)	2.5(2)
C17	0.6453(14)	0.1763(11)	-0.0341(16)	4.6(4)
C18	0.6709(15)	0.2044(12)	-0.1155(19)	5.3(5)
C19	0.7163(17)	-0.0814(13)	0.242(2)	6.5(7)

C20	0.8799(16)	0.2533(15)	-0.0187(18)	5.4(5)
C21	0.952(5)	0.233(8)	0.083(4)	32(7)
C22	0.6746(19)	-0.0197(14)	0.3379(18)	7.0(9)

Table 1. Atomic coordinates and B_{iso}/B_{eq} (continued)

atom	x	y	z	B_{eq}
C27	0.6599(8)	0.0370(9)	0.1709(11)	2.7(3)
C28	0.7381(11)	0.1930(12)	0.3939(11)	3.5(3)
C31	0.7826(9)	0.2667(10)	0.3706(11)	2.8(3)
C32	0.6602(15)	0.0927(15)	-0.1530(14)	4.9(4)
C37	0.965(4)	0.693(4)	0.304(4)	10.9(14)
C39	0.7954(8)	0.2894(8)	0.2788(11)	2.5(2)
C40	0.905(4)	0.634(4)	0.236(5)	12.8(19)

B_{eq} = 8/3 $p^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}(aa^*bb^*)\cos g + 2U_{13}(aa^*cc^*)\cos b + 2U_{23}(bb^*cc^*)\cos a)$

Table 2. Atomic coordinates and B_{iso} involving hydrogen atoms

atom	x	y	z	B_{iso}
H4	0.81679	0.33315	0.56208	5.394
H5	0.61920	0.11705	0.11255	3.491
H6	0.84555	0.36576	0.42100	4.110
H8	0.69273	0.17802	-0.22734	5.616
H9	0.74538	0.20594	0.59436	5.323
H10	0.62337	0.01664	-0.06748	4.163
H11	0.70157	0.12705	0.49700	5.755
H14A	0.81418	0.05489	0.20840	8.962
H14B	0.81492	0.04301	0.30767	8.962
H14C	0.78455	0.09193	0.27149	8.962
H15A	0.77679	0.12444	-0.01215	7.332
H15B	0.81310	0.08909	0.04312	7.332
H15C	0.84586	0.12316	-0.04676	7.332
H17	0.64074	0.20545	0.00744	5.465
H18	0.68353	0.25208	-0.12977	6.381
H19A	0.74182	-0.07765	0.18910	7.831
H19B	0.66704	-0.12143	0.23756	7.831
H19C	0.74073	-0.08970	0.28854	7.831
H20A	0.90272	0.30120	0.00646	6.469
H20B	0.83287	0.24133	-0.04111	6.469
H20C	0.91003	0.25246	-0.06434	6.469
H21A	0.95284	0.19946	0.12476	38.821
H21B	0.96792	0.27924	0.10973	38.821
H21C	0.98527	0.23881	0.03702	38.821
H22A	0.69854	-0.02751	0.38570	8.408
H22B	0.62524	-0.05956	0.33388	8.408
H22C	0.67418	0.02521	0.34606	8.408
H23	0.75532	0.19180	0.22734	3.036
H24	0.60943	-0.01094	0.07092	3.362
H28	0.71545	0.15671	0.35251	4.242
H32	0.66678	0.06473	-0.19437	5.876

H39	0.84450	0.33216	0.27412	3.013

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